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EXAMINER
SITTON, JEHANNE SOUAYA

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/087,411	SCHROTH, GARY P.	
	Examiner	Art Unit	
	Jehanne Souaya Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner reviewing your application at the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to examiner Jehanne Sitton.

2. Currently, claims 1-12 are pending in the instant application. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance.

3. The rejection of claims 6-12 under 35 USC 103(a) made in the previous office action is withdrawn in view of the new grounds of rejection of such claims under 35 USC 102(b). The rejection of claims 1-5 under 35 USC 102(b) made in the previous office action is maintained and set forth below. Response to applicant's arguments follows it. As the instant office action contains new grounds of rejection, the finality of the previous office action is withdrawn. The following office action is NON-FINAL.

Claim Interpretation

4. The claims must be interpreted before proceeding with the prior art analysis. Here, the central question is what is the meaning of the terms "coded test unit" or "plurality of coded test units" and "decoding oligonucleotide". The terms are defined in the specification as follows:

"Coded test unit" is defined as a test unit comprising a coding oligonucleotide, or a test unit linked to a coding oligonucleotide (page 8). Looking to the specification at page 8, a test unit is defined as any unit that can comprise a test moiety. Therefore, given the definitions in the specification, a "coded test unit" is any unit that comprises a test

moiety and a coding oligonucleotide. Again, looking to the specification, the term "test moiety" is defined as a moiety that can be assayed for a desired property and the term "coding oligonucleotide" is defined as an oligonucleotide that can be used to identify a test unit. A claim limitation is read in light of express definitions of the specification, so the definition of the term "coded test unit" requires a "unit" that comprises some "moiety" and an oligonucleotide. The term "unit" is not defined and the term moiety can be any atom, nucleotide, or oligonucleotide for example. It is noted, however, that limitations from the specification are not read into the claims. Therefore, any preferred embodiments or examples of such terms, (ie on page 7, when referencing "test moiety" the specification states at lines 33-34 "for example a test moiety can be assayed for an interaction with a target moiety") are not limitations which are read into the claims. Therefore, the term will be read only in light of the express definition given in the specification and will not be read with any of the structural preferences set forth in the specification. Therefore, given the broadest reasonable interpretation, a coded test unit need only comprise an oligonucleotide linked to a moiety [which can be any atom, nucleotide, or oligonucleotide for example]. In other words, a coded test unit can be nothing more than an oligonucleotide linked to an oligonucleotide, for example the oligonucleotide sequence ATTGGC is comprised of a first oligonucleotide ATT (the test moiety) and a second oligonucleotide GGC (the coding oligonucleotide). A "plurality" of coded test units are therefore broadly interpreted to be more than one coded test unit or in other words, more than one oligonucleotide linked to a moiety [which can be any atom, nucleotide, or oligonucleotide for example], or even more broadly, more than one oligonucleotide.

A "decoding oligonucleotide" is defined as an oligonucleotide that can be used to decode a test unit. Decode is defined as identifying (page 7), therefore, the broadest reasonable interpretation of the term is an oligonucleotide that is used to identify a test unit [which is a unit which can comprise an oligonucleotide (moiety) linked to an oligonucleotide].

The term "coding" is defined as a method of incorporating (the specification does not state how) a coding oligonucleotide (which can be used to identify a test unit) in a test unit.

The term "solid substrate" is not defined. However, the term "substrate" is defined as any solid support capable of having a code oligonucleotide and/or test moiety immobilized thereon. It is noted that the term has not been defined to actually have a code oligonucleotide and/or test moiety immobilized thereon. In other words, the substrate need only be made of a material capable of such.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 and 4 recite the limitation "wherein the [plurality of] coded test unit[s] is coded with a decoding oligonucleotide". The specification defines coding as a method of

incorporating a coding oligonucleotide in a test unit. Claims 3 and 4 are dependent from claim 1, however, it is unclear how claim 3 further defines claim 1 because in claim 1, the decoding oligonucleotide is contacted with a test unit that has *already* been coded, and as such is termed a 'coded test unit' in claim 1. However, because of the dependency of claims 3 and 4, it is unclear what type of structure would be a 'coded test unit' in claim 1, and the metes and bounds of the structures of test units, coded test units, and coding oligonucleotides (which are contained in a coded test unit) specifically in claims 1, 3, and 4 are unclear. Due to the dependency from claims 1, 3, or 4, claims 2, and 5-12 are also indefinite.

Claim 6 is indefinite as it is unclear how a coded test unit can 'comprise' a solid support. It is unclear if in such case, the coded test unit comprises the solid support and a bound oligonucleotide or oligonucleotides, or if the oligonucleotides surround, are linked to, or are surrounded by a substrate.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Benner (US Patent 5,432,272).

With regard to claims 1-2, Benner teaches a method wherein different oligonucleotides containing orthogonal bases (see col. 6-10, examples 1 and 2 and figure

5) (decoding oligonucleotide) and 8 mers or 18mers (coded test unit) are contacted, and then the 8mers or 18mers are elongated using either T7 RNA polymerase or DNA polymerase with dNTPs and orthogonal bases, X or iso G, such that some of the 8mer or 18 mers comprise an orthogonal nucleotide. The coded test unit is the 8 mer or 18 mer and comprises a test unit which comprises a test moiety, for example with regard to the 8 mer, the GATT sequence, and a coding oligonucleotide, the TTGA sequence. Thus the coded test unit has been contacted with a decoding oligonucleotide, and hybridization and elongation of the coded test unit has occurred (the test moiety has been assayed for a detectably property). In either panel of figure 5, the reactions comprise both a plurality of coded test units as well as a first molecule and a second molecule. A detectable signal is produced, (see col. 8, lines 10-15 and col. 9, where Benner teaches that products were analyzed by gel electrophoresis and autoradiography).

It is noted that specifically with regards to claims 1-4, the metes and bounds of structures which can be considered a "test unit" or a "coded test unit" are unclear (see 112/2nd rejection above). Due to the dependency of claims 3 and 4 from claim 1, the claims can be alternatively interpreted such that the coded test unit appears not to actually have been coded (that is to contain a coding oligonucleotide) prior to the contacting step but could be 'coded' during the actual step of 'contacting'. In such case, the 8 mer or 18 mer of Benner is the test unit and the test moiety, and the coding oligonucleotide is incorporated in the test unit, that is the test unit is 'coded' once the 'decoding oligonucleotide' and polymerase have been contacted to the test unit. In such case, the method of Benner teaches that the 'coded test units' are "coded" by the decoding oligonucleotides as Benner teaches that with decoding oligonucleotides containing iso-C,

only full length products were obtained when d-isoG was present in the incubation mixture (claims 3-5).

With regard to claim 6, the claim does not make clear how a coded test unit, which can be an oligonucleotide based on the definitions in the specification, can 'comprise' a substrate. It is unclear if the oligonucleotides surround, are linked to, or are surrounded by a substrate. Therefore, the claim has been interpreted to encompass any of the instances. In the instant case, the reaction container that the reaction taught by Benner is carried out in can be considered a solid substrate. Therefore, with regard to claim 7, each of the different 8 mer and 18 mers can be considered a first substrate and a second substrate, respectively. The claim does not require that the coded substrates are contained within the same mixture. With regard to claim 12, the term 'array' has not been specifically defined by the specification. The term "array" can mean a collection of things, as defined by encarta.msn.com: "collection: a large number or wide range of people or things". In the instant case the different reactions samples can be considered in a collection or in an array.

With regard to the recitation of 'polynucleotide' and 'oligonucleotide' the specification teaches at page 5 that the terms can be used interchangeably. Because claim 1 can be interpreted differently due to the broad terms and dependency of claims 3 and 4, the same is true for claims 8-11. In the first instance, with regard to claim 8, the 8 and 18mers taught by Benner can each be considered to be a test moiety which is an oligonucleotide (claim 9). In the step of incorporating the 'coding oligonucleotide' by elongation of the test moiety with a polymerase to achieve a longer nucleic acid molecule, such nucleic acid molecule can be considered a single polynucleotide that

comprises the test moiety and the coding oligonucleotide (claim 10), or the test moiety can be considered an oligonucleotide or first polynucleotide and the coding oligonucleotide can be considered a second polynucleotide (claim 11). In a second instance, with regard to claim 8, using the 8 mer as an example: the GATT sequence can be the test moiety which is an oligonucleotide (claim 9), the TTGA can be the coding oligonucleotide and the full 8 mer can be a single polynucleotide (claim 10) or the GATT can be a first polynucleotide and the TTAG can be a second polynucleotide (claim 11).

Response to Arguments

9. The response traverses the rejection. The response at pages 4-10 asserts that Benner does not teach each and every element of the claimed invention. The response reiterates the teachings of Benner and then states in each instance that Benner does not teach the exact wording of each of the instant claims. The response does not state how it is interpreting the claims to be different from the teachings of Benner but simply quotes exact terms from the claims and states that Benner does not teach such terms. It therefore appears that the response asserts that because Benner does not use the exact wording of the instant claims, that Benner cannot anticipate the claims. This argument as well as each of Benner's teachings have been thoroughly reviewed in light of the claims, however this argument is not found persuasive. As noted above, the claims use very broad wording that is only generally defined by the specification. Additionally, the definitions in the specification use terms to define themselves (for example a test unit is defined as a unit comprising a test moiety and either comprising or linked to an oligonucleotide that can be used to identify a test unit), and the dependency of the claims is unclear such the metes and bounds of the structures in both the dependent and

independent claims are unclear. Taking the very broad definitions from the specification, the claims were interpreted and compared to the teachings of Benner as outlined above. For the reasons set forth in the rejection above, the terms used in the claims are not sufficient to distinguish the claimed methods from the teachings of Benner.

10. Claims 1-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Collins et al (hereinafter referred to as Collins; US Patent 5,681,702).

Collins teaches a nucleic acid sandwich assay of hybridizing nucleic acids on a solid support to detect a target polynucleotide of interest, wherein the method occurs on a solid support which have capture probes bound to the surface wherein incubation is carried out with a target nucleic acid molecule, nucleic acid capture extenders (CE), and nucleic acid label extenders (LE) (abstract, para bridging cols 9 and 10 and figure 1). Collins teaches the method then involves optionally adding a nucleic acid amplification multimer under conditions such that the multimer will hybridize to the LE. Collins then teaches that labeled nucleic acid probes are added such that the labeled probe hybridizes to either the LE (in the absence of an amplification multimer) or the amplification multimer. Looking to figure 1, the capture probe (CP) hybridizes to CE (this is designated as C-2/C-3) which hybridizes to target (designated C-1). The target hybridizes to the LE (designated L-1), which hybridizes to the amplifier (designated L-2/M-1). The amplifier hybridizes to the labeled probe (LP) (designated M-2/L-3). With regard to instant claim 5 (orthogonal nucleobase is iso-C or isoG) Collins teaches that the hybridizing nucleotide segments contain nucleotide units other than A, T, C, G, and U, such as isoG and isoC (orthogonal nucleotides; see col. 11, lines 12-15; col, 4, lines 55-

56; col. 6, lines 24-55). Collins teaches that these non natural bases which form unique base pairs may be incorporated in complementary nucleic acid sequences C-2/C-3, L-2/M-1, and L-3/M-2 (see figure 1; col. 11, lines 18-30). Collins teaches that the assay can involve a plurality of capture probes affixed to the solid surface and that the incorporation of non natural bases will minimize non specific hybridization (see col. 12, lines 32-43).

With regard to claims 1 and 6, the decoding oligonucleotide comprising an orthogonal nucleobase is the labeled probe and the coded test unit can be the complex of the solid support bound to the capture probe, the CE, target, LE, and optionally the amplifier. In such case, as taught by Collins, the LP (decoding oligonucleotide) is 'contacted' with the coded test unit which comprises a solid support. With regard to claim 2, the first and second molecules are considered the CE and the target, respectively, or the target and the LE, respectively, for example. Such are inherently 'identified' in the method of Collins. Alternatively, as Collins teaches that a plurality of capture probes can be bound to the solid support, the target in the hybridization complex of capture probe 1 can be considered the first molecule and the target in the hybridization complex of capture probe 2 can be considered the second molecule. With regard to claim 7, the plurality of capture probes bound to solid support are a plurality of coded substrates and the identification of target in each capture probe complex is considered identifying a first substrate and a second substrate. The specification does not define the term 'array'. The plurality of coded substrates are inherently 'arrayed' (claim 12). With regard to claim 8, each coded substrate comprises a test moiety (target) which is an oligonucleotide (claim 9). As such, a single polynucleotide comprises the test moiety and the coding

oligonucleotide (claim 10). Alternatively, the target is considered the test moiety and the coding oligonucleotide is considered the LE or the amplifier (claim 11 wherein the first polynucleotide comprises the test moiety and the second polynucleotide comprises the coding oligonucleotide).

As noted in the previous rejection and the rejection under 112/2nd paragraph, with regard to claims 3 and 4, it is unclear how the decoding oligonucleotide can code a structure which has already been defined as 'coded' in Alternatively, with regard to claims 1, 3, 4, and 6: the decoding oligonucleotide is considered the amplifier or LE, the coding oligonucleotide is the labeled probe (LP) (claim 11) and the coded test unit is the CP bound to a solid support, wherein the CP is hybridized to the CE which is hybridized to target (test moiety which is an oligonucleotide, claims 8 and 9). In such case, the decoding oligonucleotide, amplifier or LE, which Collins teaches comprises an orthogonal base (claim 5), 'codes' the coding oligonucleotide as the LP has been incorporated into the test unit and identifies the test unit (claims 3 and 4). With regard to claim 2, as Collins teaches that a plurality of capture probes can be bound to the solid support, the target in the hybridization complex of capture probe 1 can be considered the first molecule and the target in the hybridization complex of capture probe 2 can be considered the second molecule. With regard to claim 7, the plurality of capture probes bound to solid support are a plurality of coded substrates and the identification of target in each capture probe complex is considered identifying a first substrate and a second substrate. The specification does not define the term 'array'. The plurality of coded substrates are inherently 'arrayed' (claim 12). With regard to claim 10, the LP can also be considered to comprise both the test moiety and the coding oligonucleotide.

Conclusion

11. No claims are allowable over the cited prior art.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (571) 272-0507.

Jehanne Sitton
Primary Examiner
Art Unit 1634
4/20/04